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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/973,958	10/11/2001	Martin J. Macphee	CI-0015	5803

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FLESHNER & KIM, LLP
P.O. BOX 221200
CHANTILLY, VA 20153

EXAMINER	
MCKANE, ELIZABETH L	

ART UNIT	PAPER NUMBER
1744	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/973,958	MACPHEE ET AL.	
	Examiner	Art Unit	
	Leigh McKane	1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *104-261* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *121-139,144-147 and 152-173* is/are allowed.

6)☒ Claim(s) *104-120,140-143,148-151 and 174-261* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *092503* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 104-111, 113-115, and 117-120 are rejected under 35 U.S.C. 102(b) as being anticipated by Peterson (U.S. Patent No. 5,730,933) in view of Wiesehahn et al (U.S. Patent No. 4,727,027).

Peterson teaches the use of e-beam or gamma radiation to sterilize a biological material (blood, serum, tissues, demineralized bone matrix, etc.) that is sensitive to radiation, wherein a stabilizer (antioxidant/free-radical scavenger, such as ascorbate or propyl galate) is added to the material prior to irradiation and the material is then irradiated "under standard sterilization conditions...at an intensity and for a time duration sufficient to destroy substantially all of the microorganism contamination" (col.4, lines 59-64). See also col.4, lines 36-51; col.6, lines 1-18. The material may also be lyophilized or dried with drying agents and/or frozen and placed under a vacuum or inert gas, such as nitrogen or argon (col.4, lines 51-58; col.5, lines 28-35 and lines 53-67. Peterson is silent with respect to adding a ligand to the biological material before irradiation.

Wiesehahn et al teaches a method of sterilizing blood products wherein a stabilizing ligand, heparin, is added to the material before irradiation. Wiesehahn et al discloses that the addition of heparin controls "any activated clotting factors" (col.11, lines 31-33) in the biological material. For this reason, it would have been obvious to add heparin to the blood products being

sterilized in the method of Peterson.

3. Claims 104-107, 109, 110, 112, and 116, 117, 119, and 120 are rejected under 35 U.S.C. 102(b) as being anticipated Odland (U.S. Patent No. 5,989,498) in view of Wiesehahn et al.

Odland teaches the sterilization of sensitive biological materials (heart valves, homograft tissues, etc.) at ambient temperature to slightly above ambient (col.4, lines 35-37 and 48-51) with e-beam radiation. Prior to radiation, the biological material is stabilized (cross-linked) with a stabilizer mixture (cross-linking agents) and the pH is adjusted. See col.7, lines 4-19 and lines 38-58. The material is then irradiated with e-beam radiation at a dose rate of 2.2×10^4 kGy/hr (col.3, line 24). Odland is silent with respect to adding a ligand to the biological material before irradiation.

Wiesehahn et al teaches a method of sterilizing blood products wherein a stabilizing ligand, heparin, is added to the material before irradiation. Wiesehahn et al discloses that the addition of heparin controls "any activated clotting factors" (col.11, lines 31-33) in the biological material. For this reason, it would have been obvious to add heparin to the biological materials being sterilized in the method of Odland, especially those materials containing blood products (heart valves, tissues, vessels, etc.).

4. Claims 104-107, 110-114, and 116-118 are rejected under 35 U.S.C. 102(b) as being anticipated by Horowitz et al (U.S. Patent No. 5,712,086) in view of Wiesehahn et al.

Horowitz et al teaches mixtures of sensitive biological materials with stabilizer mixtures

and sensitizers that ultimately undergo radiation sterilization. See Abstract. The stabilizer can be glutathione or vitamins, among others (col.7, lines 3-8). The biological material may be blood, blood products, immunoglobulins, etc.. (col.5, line 63 to col.6, line 36). Horowitz et al discloses exposing the materials to particular fluences of radiation (col.6, lines 48-65) for particular time periods (col.7, lines 45-46) and at a temperature slightly above ambient to frozen (col.6, lines 41-48). Radiation sources include UV, gamma, x-rays, and visible light. Horowitz et al is silent with respect to adding a ligand to the biological material before irradiation.

Wiesehahn et al teaches a method of sterilizing blood products wherein a stabilizing ligand, heparin, is added to the material before irradiation. Wiesehahn et al discloses that the addition of heparin controls "any activated clotting factors" (col.11, lines 31-33). For this reason, it would have been obvious to add heparin to the blood products being sterilized in the method of Horowitz et al.

6. Claims 148-151 are rejected under 35 U.S.C. 102(b) as being anticipated by Odland.

Odland teaches the sterilization of sensitive biological materials (heart valves, tissues, etc.) at ambient temperature to slightly above ambient (col.4, lines 35-37 and 48-51) with e-beam radiation. Prior to radiation, the biological material is stabilized (cross-linked) with a stabilizer mixture (cross-linking agents) and the pH is adjusted. See col.7, lines 4-19 and lines 38-58. The material is then irradiated with e-beam radiation at a dose rate of 2.2×10^4 kGy/hr (col.3, line 24). After sterilization the tissues are more pliable, have a greater range of movement, and have an increased durability over non-irradiated tissues. See col.8, lines 47-51.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 140-143 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson or Odland, both in view of Salim-Hanna et al (Abstract of "Free radical scavenging activity of carnosine").

Both of Peterson and Odland teach a method of sterilizing a biological material wherein a stabilizer is added to the material prior to irradiation. Neither of Peterson or Odland teach adding a dipeptide stabilizer. Salim-Hanna et al teaches that the addition of carnosine, a dipeptide stabilizer to peroxidase and lysozyme prior to irradiation, prevents free radical damage thereto. Therefore, it would have been obvious to add carnosine to the biological products of Peterson and Odland prior to irradiation in order to prevent free radical damage.

9. Claims 140, 141, 143, and 174-177 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horowitz et al in view of Salim-Hanna et al.

Horowitz et al teaches mixtures of sensitive biological materials with stabilizer mixtures and sensitizers that ultimately undergo radiation sterilization. See Abstract. The stabilizer can be ascorbate, alone or in combination with other stabilizers. The biological material may be blood, blood products, immunoglobulins, etc.. (col.5, line 63 to col.6, line 36). Horowitz et al fails to teach adding a dipeptide stabilizer. Salim-Hanna et al teaches that the

addition of carnosine, a dipeptide stabilizer to peroxidase and lysozyme prior to irradiation, prevents free radical damage thereto. Therefore, it would have been obvious to add carnosine to the biological products of Horowitz et al prior to irradiation in order to prevent free radical damage. Moreover, it would have been obvious to combine the carnosine with other stabilizers used by Horowitz et al, such as ascorbate, as Horowitz et al teaches using stabilizers in combination.

New Matter

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 178-261 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the specification does not provide sufficient support for the limitation in claims 178 of "said effective rate is not constant and comprises a rate of between about 0.1 kGy/hr to 3.0 kGy/hr for at least a portion of said period of time and a rate of at least 6.0 kGy/hr for at least another portion of said period of time."

Although Applicant points to paragraphs 113-119 of the specification, the Examiner has found no support in these paragraphs. The only teaching these paragraphs give with respect to

the dose rate is that preferably the dose rate is constant but when a constant dose rate is impractical or not desired a non-constant dose rate can be used (paragraph 113). However, in none of paragraphs 113-119, or elsewhere in the specification, is there guidance as to what different dose rates should be chosen when the dose rate is not constant.

Moreover, although these limitations were allowed in U.S. Patent No. 6,682,695, the Examiner notes that the limitations in questions were present in original claims 1 and 2 of the above patent, and thus had support in the original disclosure.

Allowable Subject Matter

12. Claims 121-139, 144-147, and 152-173 are allowed.

Conclusion

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh McKane whose telephone number is 571-272-1275. The examiner can normally be reached on Monday-Wednesday (7:15 am-4:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert J. Warden can be reached on 571-272-1275. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leigh McKane

Leigh McKane
Primary Examiner
Art Unit 1744

elm
22 March 2004